Differential diagnosis of childhood abdominal mass

- Renal masses
  - Wilm's tumour
  - Multicystic dysplastic kidney
  - Large hydronephrosis
  - Polycystic kidney
  - Congenital mesoblastic nephroma (< 1 yr)
- Non-renal masses
  - Mesenteric and choledochal cysts
  - Intestinal duplication cysts
  - Splenomegaly
  - Neuroblastoma
  - Rhabdomyosarcoma
  - Lymphoma
  - Hepatoblastoma

Wilm's tumour (nephroblastoma)

First described by Max Wilms in 1889
Abnormal proliferation of metanephric blastema without differentiation into glomeruli or tubules
Incidence 1:150,000 (7 per million children per year)
6-7% of all childhood cancers
Comonest renal malignancy
Commonest cause of solid abdominal malignancy
Peak age 3-4 yrs
Blacks > whites
Equal sex ratio
90% sporadic; 10% a/w 'predisposition syndromes' (see below):

Denys-Drash	WT, glomerulosclerosis and ambiguous genitals
WAGR	WT, aniridia, GU malformation, retardation
Beckwith-Weidemann	WT, macroglossia, visceromegaly, omphalocoele
Horseshoe kidney	7-fold increased risk

95% unilateral; 5% bilateral (more common in above syndromes)
Overall 90% 5YS with combination of surgery, chemotherapy and occasionally radiotherapy
Presentation

- Painless abdominal mass
- Haematuria in 10%
- Occasionally left varicocoele
- Rarely rupture and acute abdomen

Pathology

- Molecular
  - WT1 gene on 11p13 (DDS, WAGR)
  - WT2 gene on 11p15 (BWS)
  - Loss of 1p and 16q associated with increased likelihood of relapse and death

Macroscopic
- Unicentric with pseudocapsule of compressed normal parenchyma
- Friable, with tendency to rupture

Microscopic
- Classic good prognosis Wilm's has 'triphasic' appearance: blastema, tubular cells and stroma
- Poor prognosis WT associated with anaplastic, rhabdoid, or clear-cell sarcoma (10% tumours; 60% deaths). NB. some authors do not believe that rhabdoid and clear-cell sarcoma subtypes true Wilm's.
- 30-40% of WT kidneys contain nephrogenic rests – islands of abnormally persistent nephrogenic (blastema) cells thought to be the precursor lesions from which WT develops

Investigation

USS with Doppler	mass and renal vein/IVC invasion
CT C/A/P	standard cancer staging
Urinalysis	proteinuria = ?DDS
	VMA = ? neuroblastoma
CT head	Rhabdoid and clear cell sarcoma only
Bone scan	Rhabdoid and clear cell only
Clotting screen	TEG vs. APTT and bleeding time
	Anti-vWF agents from tumour

Staging (Children's Oncology Group)

Stage	
I	Tumor limited to the kidney and completely excised. The renal capsule is intact and the tumor was not ruptured prior to removal. There is no residual tumor.
II	Tumor beyond the kidney, but is completely resected. Extrarenal vessels may contain tumor thrombus or be infiltrated by tumor.
III	Residual nonhematogenous tumor confined to the abdomen: lymph node involvement, any tumor spillage, rupture or biopsy, peritoneal implants, tumor beyond surgical margin either grossly or microscopically, or tumor not completely removed.
IV	Hematogenous metastases to lung, liver, bone, brain, etc.
V	Bilateral renal involvement at diagnosis.

Management
- Trimodal therapy with surgery, chemo and RT
- Chemotherapy = VAD (vincristine, actinomycin D, doxorubicin)
- General strategy is to identify high risk patients for maximal treatment while sparing low-risk patients highly toxic anthracyclines (doxorubicin) and radiotherapy
- Differing treatment philosophies across Atlantic: US surgery first.
- UK = Pre-operative chemotherapy (4 weeks) designed to downstage tumour and reduce risk of rupture; then surgery followed by adjuvant chemotherapy [Stage 1 = V; Stage 2 = V + A; Stage 3 + = V + A + D]
- Abdominal radiotherapy reserved for gross abdominal disease, anaplastic subtype, and chemotherapy failures

Prognosis
- Poor prognostic factors
  - Anaplastic features

Advanced stage
Tumour spillage
Lymph node metastases

Survival

Good prognosis

Stage 1/2	90%	5YS
Stage 3	80%	5YS
Stage 4	70%	5YS
Stage 5	70%	5YS

Poor prognosis

Clear cell	75%	5YS
Anaplastic	60%	5YS
Rhabdoid	20%	5YS

Rhabdomyosarcoma

Rare tumour of mesenchyme, resembling skeletal muscle
10-15% solid childhood malignancies
One third involve GU tract, typically bladder base, prostate, paratesticular, uterus & vagina
Paratesticular rhabdomyosarcoma accounts for 10% solid scrotal mass lesions in childhood
Incidence 1 in 2 million
Males > females
Blacks > whites
Increased risk in Li Fraumeni syndrome (p53 mutation)
Embyronal, alveolar and pleomorphic forms: embryonic good prognosis; almost all bladder tumours embyonal
GU rhabdomyosarcoma
Irritative bladder symptoms
Protruding vaginal mass
Combination of surgery, chemotherapy and RT
Surgery often first line, but debulking preferred to radical excision if continence mechanisms likely to be involved
70-80% 5YS

Neuroblastoma

Most common extracranial childhood tumour
Arise from neuroectoderm – 50% adrenal medulla, remainder along sympathetic chain
Incidence 1:100,000
Median age at diagnosis 2 yrs
Unlike Wilm's, patients present with abdominal pain and systemic features
Occasionally proptosis and periorbital ecchymosis 2' retro-orbital mets
Urinary homovanillic acid (HVA) and vanillylmandelic (VMA) elevated in 90%
Metaiodobenzylguanidine (MIBG) scans highly sensitive. Diagnosis a combination of MIBG and stndard staging investigations
Survival generally poor except for a subset with favourable features (low stage, +/- mets limited to skin, liver and bone marrow (stage 4S))
Poor prognostic features:

High VMA:HVA ratio
Elevated serum ferritin and neuron-specific enolase
Amplification of N-myc oncogene
Deletion of short-arm of chromosome one
Adrenal location